

CURRICULUM VITAE

Name : DIVITA Gilles

Birth : April 28th, 1962 in Lyon (France).

Nationality : French

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UNIVERSITY TRAINING

1985 – 1988: University training at the University Claude Bernard, Lyon, France.

1991: Ph.D. in Biochemistry awarded with First Class Honors.

"Structure and function of the *Schizosaccharomyces pombe* mitochondrial F1-ATPase"

Awarded a prize from the **DINA SURDIN foundation** for the best Ph.D. in Biochemistry.

PROFESSIONAL EXPERIENCE

1987-1991: PhD in Biochemistry

Biology and Technology of Membranes and of Integrated Systems, UMR 24, CNRS

Université Claude Bernard - LYON I. Director : Prof. D. C. GAUTHERON

1991-1993 : Post-Doctoral position

Max Planck Institut of Medical Research, Department of Biophysics, Jahnstrasse 29,

D-69120 Heidelberg, Germany. Director : Prof. R. S. GOODY.

Project: Structure and mechanism of HIV reverse transcriptase .

1993-1995: Leader group position at Max Planck Institute of Medical Research, Department of Biophysics, Director : Prof. K. HOLMES

1996 - 2001: Principal Investigator (CR1 –CNRS) at the Centre de Recherche en Biochimie Macromoléculaire, Biophysics Department, UPR 1086 CNRS, Montpellier, France.

1999-2001: Associated Professor (Visiting scientist) at the **Scripps Research Institute**, La Jolla, USA. Laboratory of **Prof. J.A. Tainer**, Molecular Biology Department

Since 2002: Research Director at the Centre de Recherche en Biochimie Macromoléculaire, Biophysics Department, UPR 1086 CNRS, Montpellier France.

Principal Research Projects:

- 1 - Design and development of peptides for gene and protein delivery
- 2 - Control of the cell cycle progression and design of inhibitors

3 – Regulation of HIV infection by targeting reverse transcriptase activation

PUBLICATIONS

- 1 - Morris, M.C., Gondeau, C., Tainer, J. A., & Divita G. Kinetic mechanism of activation of the Cdk2/cyclin A complex : Key role of the C-lobe of the Cdk. **J. Biol. Chem.** (2002), 277, 23847-23853
- 2 - Morris, M.C., Chaloin, L., Heitz, F., & Divita G. Signal sequence based cell penetrating peptides (NLS) and their applications for gene delivery. **Cell Penetrating Peptide Handbooks**, CRC press, (2002), 5, 93-114
- 3 - Chaloin, L., Van Mau, N., Divita, G., & Heitz, F. Interactions of cell penetrating peptides with membranes. **Cell Penetrating Peptide Handbooks**, CRC press. (2002), 8, 163-187
- 4 - Morris, M.C., & Divita G. Dimerization of HIV reverse transcriptase : a new target for the design of HIV inhibitors. **Current Drug Targets** (2002) *sous presse*
- 5 - Rittner, K., Benavente, A., Bompard-Sorlet, A., Heitz, F., Divita, G., Brasseur, R. & Jacobs, E. New basic membrane-destabilizing peptides for plasmid-based gene delivery *in vitro* and *in vivo*. **Mol. Ther.** (2002) 5, 104-114.
- 6 - Morris, M.C., Depollier, J., Mery, J., Heitz, F. & Divita G. A peptide carrier for the delivery of biologically active proteins into mammalian cells. **Nature Biotechnol.** (2001), 19, 1173-1176.
- 7 - Bertolaet, B., Clark, D., Wolff, M., Watson, M., Reed, S & Divita, G. UBA domains mediate Protein-protein interactions between two DNA damage inducible proteins **J. Mol. Biol.** (2001), 313, 955-963
- 8 - Bertolaet, B., Clark, D., Wolff, M., Watson, M., Divita, G., & Reed, S. UBA domains of DNA damage inductible proteins interact with ubiquitin **Nature Struct. Biol.** (2001), 8, 417-422
- 9 - Morris M.C., Heitz A, Mery J, Heitz F, & Divita G. An essential phosphorylation-site domain of human cdc25C interacts with both 14-3-3 and cyclins. **J Biol Chem.** (2000) 275, 28849-28857.
- 10 - Marthinet E, Divita G, Bernaud J, Rigal D, Baggetto LG. Modulation of the typical multidrug resistance phenotype by targeting the MED-1 region of human MDR1 promoter. **Gene Ther.** (2000) 23, 1224-33.
- 11 - Van Mau N, Misse D, Le Grimmellec C, Divita G, Heitz F, Veas F. The SU glycoprotein 120 from HIV-1 penetrates into lipid monolayers mimicking plasma membranes. **J Membr Biol.** (2000) 177, 251-257.

- 12 - Morris MC, Chaloin L, Heitz F, & Divita G. Translocating peptides and proteins and their use for gene delivery. *Curr Opin Biotechnol.* (2000) 11, 461-466.
- 13 - Chaloin, L., Morris, M.C., Van Nau, N., Mery, J., Divita, G. & Heitz, F. Synthetic primary amphipathic peptides as tools for the cellular import of drug and nucleic acids. *Current Topics in Peptide and Protein Research.* (1999), 1, 117-133.
- 14 - Morris, M.C., Heitz, F., & Divita G. Molecular mechanism of formation of cdk/cyclin complexes : role in cell cycle progression. *Recent Res. Dev. Biochemistry,* (1999), 1, 117-132
- 15 - Shafiee, M., Gosselin, G., Imbach, J.L., Divita, G., Eriksson, S., & Maury, G., Study of human deoxycytidine kinase binding properties using intrinsic fluorescence or new fluorescent ligands. *Eur. J. Med Chem.* (1999), 34, 423 - 431.
- 16 - Morris, M.C., Chaloin, L., Mery, J., Heitz, F., & Divita, G., A novel strategy for gene delivery using peptide vectors, (1999), *Eurocancer-99*, Ed. John Libbey Eurotext, Paris, 149 – 150.
- 17 - Chaloin, L., Van Mau, N., Mery, J., Divita, G., & Heitz, F. Synthesis of a template associated peptide designed as a transmembrane ion channel former. *J. Peptides Science* (1999), 5, 381-391
- 18 - Brown, N., Noble, N.E., Lawrie, A., Morris, N.C., Tunnah, P., Divita, G., Johnson, L.H. & Endicott, J. Effect of phosphorylation of Thr¹⁶⁰ on cyclin dependent kinase 2 structure and activity. *J. Biol. Chem.* (1999) 274, 8746 – 8756
- 19 - Morris, M.C., J. Mery, Heitz, A., F. Heitz & G. Divita. Design and synthesis of a peptide derived from position 195-244 of human Cdc25C phosphatase. *J. Peptides Science*, (1999) 5, 263-271
- 20 - Morris, M.C., Chaloin, L., Mery, J. Heitz, F., & Divita G., A novel potent strategy for gene delivery using a single peptide vector as a carrier. *Nucleic Acid Research* (1999) , 27, 3510 – 3517.
- 21- Morris, M.C., Berducou, C., Mery, J., Heitz, F., & Divita G., The thumb domain of the p51 subunit is essential for activation of HIV-1 reverse transcriptase. *Biochemistry*, (1999), 38, 15097 - 15103.
- 22 - Morris, M.C., Robert-Hebmann, V., Chaloin, L., Mery, J., Heitz, F., Devaux, C., Goody, R.S. & Divita, G. A new potent HIV-reverse transcriptase inhibitor : a synthetic peptide derived from interface subunit domains. *J. Biol. Chem.* (1999), 274, 24941 – 24946.
- 23 - M.C. Morris & Divita G. Characterization of the interactions between human Cdc25C, cdks, cyclins and cdk/cyclin complexes. *J. Mol. Biol.* (1999) 286, 475-487
- 24 - Rossi, F., Labourier, E., Gallouzi, I.E., Derancourt, J., Allemand, E., Divita G. & Tazi, J. The C-

- terminal domain but not the tyrosine 723 of human DNA topoisomerase I active site contributes to kinase activity. *Nucleic Acid Research* (1998) 26, 2963 – 2970.
- 25- Labourier, E., Rossi, F., Gallouzi, I.E., Allemand, E., Divita G. & Tazi, J. Interaction between the N-terminal domain of human DNA topoisomerase I and the arginine-serine domain of its substrates determines phosphorylation of SF2/ASF splicing factor. *Nucleic Acid Research* (1998) 26, 2955 – 2962.
- 26 - Chaloin, L., Vidal, P., Lory, P., Mery, J., Lautredou, N., Divita, G., & Heitz, F. Design of carrier peptide-oligonucleotide conjugates with rapid membrane translocation and nuclear localisation properties. *Biochem. Biophys. Res. Commun.* (1998), 243, 601-608
- 27 - Vidal, P., Chaloin, L., Heitz, A., Van Mau, N., Mery, J., Divita, G., & Heitz, F. Interaction of primary amphipathic vector peptides with membranes : conformational consequences and influence on cellular localisation. *J. Membr. Biol.* (1998), 162, 259-264
- 28 - Morris, M.C., F. Heitz, & G. Divita. Kinetics of dimerization and interactions of P13^{suc1} with cyclin dependent kinases. *Biochemistry*, (1998) 37, 14257 - 14266
- 29 - Heitz F., M.C. Morris, D. Fesquet, J-C. Cavadore, M. Dorée & G. Divita (1997). Interaction of cyclins with cdks : a common mechanism. *Biochemistry*, 16, 4995-5003.
- 30 - Vidal, P, M.C. Morris, L. Chaloin, J. Mery, F. Heitz. & G. Divita (1997), Conformation of a synthetic peptide which facilitates the cellular delivery of nucleic acids, *Letter in Peptide Science*, 4, 1-4
- 31- Chaloin, L., P.Vidal, J. Mery, G. Divita & F. Heitz (1997), Synthetic peptides as carriers for cellular import of drugs, *Letter in Peptide Science*, 4, 12-18
- 32 - Pelicano, H., G. Maury, A. Elalaoui, M. Shafiee, J-L Imbach, R.S. Goody & G. Divita.(1997) Study of the substrate-binding properties of bovine liver adenosine kinase and inhibition by fluorescent nucleoside analogues, *Eur. J. Biochem.* 248,930-937
- 33 - Chaloin, L, P.Vidal, A. Heitz, N. Van Mau, J. Mery, G. Divita & F. Heitz (1997), Conformations of primary amphipathic carrier peptides in membrane mimicking environments, *Biochemistry*, 36, 11179-11187
- 34 - Vidal P., M.C. Morris, L. Chaloin, F. Heitz. & G. Divita (1997), Efficient RNA delivery into non-transformed mammalian cells by using a peptide vector Solid. *C.R. Acad. Sci. Paris*, 320, 279
- 35 - Morris, M.C., P.Vidal, L. Chaloin, F. Heitz. & G. Divita (1997), A new peptide vector for efficient

- delivery of oligonucleotides into mammalian cells. *Nucleic Acids Research*, 25, 2730-2736
- 36 - Rossi F., E. Labourier, T. Forne, **G. Divita**, J. Derancourt, JF. Riou, G. Cathala, C. Brunel & J. Tazi. (1996). Specific phosphorylation of SR protein by mammalian DNA topoisomerase I. *Nature*, 381, 80-83.
- 37 - Rittinger, K., D. Negre, **G. Divita**, M. Scarabel, R.S. Goody, A.J. Cozzzone & J-C Cortay. Isocitrate dehydrogenase kinase : Overexpression in *E.Coli* and interaction with its substrates. *Eur. J. Biochem.* (1996), 237, 247-254
- 38 - Pelicano H., **G. Divita**, A. Elalaoui, M. Shafiee, G. Maury, R.S. Goody & J-L Imbach.(1995), Ligand binding properties of bovine liver adenosine kinase. *Nucleosides & Nucleotides*. 14, 473-476
- 39 - Rittinger K., **G. Divita** & R.S. Goody. (1995), HIV reverse transcriptase nucleotide-induced conformational changes and the mechanism of inhibition by non-nucleoside inhibitors. *Proc. Natl. Acad. Sci. U.S.A.* 92, 8046
- 40 - Maury G. & **G. Divita** (1995), Les progrès récents dans la connaissance de la structure de la transcriptase inverse du VIH suggèrent-ils la conception et la synthèse de nouvelles drogues anti-SIDA. *Bull. Soc. Chim. Fr.* 132, 1095-1102.
- 41 - **Divita G.**, K. Rittinger, C. Geourjon, G. Deléage & R.S. Goody. (1995), Dimerization kinetics of HIV-1 and HIV-2 reverse transcriptase. A two step process. *J. Mol. Biol.* 245, 508-512.
- 42 - **Divita G.**, K. Rittinger, T. Restle, U. immendorfer & R.S. Goody. (1995), Conformational stability of dimeric HIV-1 and HIV-2 Reverse Transcriptases. *Biochemistry*, 34, 16337-16346.
- 43 - **Divita, G.**, J. G. Baillon, K. Rittinger, J-C. Chermann & R. S. Goody (1995), Interface peptides as structure-based Human Immunodeficiency Virus reverse transcriptase inhibitors. *J. Biol. Chem.* 270, 28642-28646.
- 44- Benzaria S., G. Maury, G. Gosselin, K. Rittinger, **G. Divita**, R.S. Goody & J-L. Imbach. (1994), Synthese of 2',3',5'-trideoxyuridine-5'-methylphosphonic acid and its diphosphate derivative. Study of interaction with HIV-1 Reverse Transcriptase. *Antiviral Chemistry and Chemotherapy* 5, 221-228.
- 45 - **Divita G.**, T. Restle, R. S. Goody, J-C. Chermann & J. G. Baillon (1994), Inhibition of Human Immunodeficiency Virus Type I Reverse Transcriptase Dimerization, Using Synthetic Peptides derived from the Connection Domains. *J. Biol. Chem.* 269, 13080-13083.

- 46 - El Alaoui A., **G. Divita**, G Maury, J-L. Imbach & R.S. Goody. (1994), Intrinsic tryptophan fluorescence of bovine liver adenosine kinase, characterization of ligand binding sites and conformational changes *Eur. J. Biochem.* 221, 839-846.
- 47 - Falson P., F. Penin, **G. Divita**, J-P. Lavergne, A. Di Pietro, R. S. Goody & D. C. Gautheron.(1993) A functional nucleotide-binding domain in the F0-F1-ATPsynthase α -subunit from the yeast *Schizosaccharomyces pombe*. *Biochemistry* 32, 10387-10397
- 48 - Jault J-M., **G. Divita**, W.S. Allison & A. Di Pietro. (1993) Glutamine¹⁷⁰-to-tyrosine substitution in yeast mitochondrial F1 β -subunit increases catalytic site interaction with GDP and IDP and produce negative cooperativity of GTP and ITP hydrolysis. *J. Biol. Chem.* 268, 20762-20767.
- 49 - **Divita G.**, T. Restle & R. S. Goody.(1993) Caracterization of the dimerization process of HIV-1 reverse transcriptase heterodimer using intrinsic protein fluorescence *FEBS Lett.*324, 153-158
- 50 - **Divita G.**, B. Muller, U. Immendörfer, M. Gautel, K. Rittinger, T. Restle & R.S. Goody (1993) Kinetics of interaction of HIV reverse transcriptase with primer/template.. *Biochemistry* 32, 7966-7961
- 51 - Bellon L., J-L.Barascut, G. Maury, **G. Divita**, R.S. Goody & J-L Imbach.(1993). 4'-thio-oligoribonucleotides : synthesis of 4'-thio-oligo-uridylates, nuclease resistance, base pairing properties and interaction with HIV-1 reverse transcriptase. *Nucl. Acids Res.* 21, 631-641
- 52 - Maury G, **G Divita**, F. Morvan, R.S. Goody & J-L. Imbach. (1993) Rapid determination of the affinity of 28 and 14 mers phosphorothioate oligonucleotides for HIV-1 reverse transcriptase. *Biochim. Biophys. Acta* 1216,1-8
- 53 - **Divita G**, R.S. Goody, D. C. Gautheron & A. Di Pietro (1993) Structural mapping of catalytic site with respect to α -subunit and noncatalytic site in yeast mitochondrial F1-ATPase. *J. Biol. Chem.* 268, 13178-13186
- 54 - Sontag B., A-M. Reboud, **G. Divita**, A. Di Pietro, D. Guillot & J-P. Reboud (1993). Intrinsic tryptophan fluorescence of rat liver elongation factor EF-2 to monitor interaction with guanylic and adenylic nucleotides and related conformational changes. *Biochemistry* 32, 1976-1980
- 55 - **Divita G.**, J-M Jault, D.C. Gautheron & A. Di Pietro (1993). Specific chemical modification of α -subunit tryptophan residues in *Schizosaccharomyces pombe* mitochondrial F1-ATPase. Correlation to nucleotide binding and enzyme activity. *Biochemistry* 32, 1017-1980
- 56 - **Divita G.**, A. Di Pietro, B. Roux & D.C. Gautheron (1992). Differential nucleotide binding to

catalytic and noncatalytic sites and related conformational changes involving a/b subunit interactions as monitored by sensitive intrinsic-fluorescence in *Schizosaccharomyces pombe* mitochondrial F1. **Biochemistry** 31, 5791-5798

57 - Divita G., A. Di Pietro, G. Deleage, B. Roux & D.C. Gautheron (1991) Intrinsic tryptophan fluorescence of *Schizosaccharomyces pombe* mitochondrial F1- ATPase. A powerful probe for phosphate and nucleotide interactions. **Biochemistry** 30, 3256-3262.

58 - Di Pietro, A., Jault, JM., Falson, P., Divita, G., & Di Pietro, A. (1989) Structure-function relationships of mitochondrial ATPase-ATP synthase using *S. pombe* yeast mutants with altered F1 subunits. **Biochimie**, 71, 931-940